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REMARKS

Claim 1 is rejected under 35 U.S.C. §112 as being indefinite.

Claims 10-11 are rejected under 35 U.S.C. §101 on the ground that the claimed invention is directed to non-statutory subject matter.

Claims 1-9 are rejected under 35 U.S.C. §103 as being obvious over the art of Malecha *et al.* (1992), Okuno *et al.* (1997) and Nagamine *et al.* (1980).

Rejection of Claim 1 under 35 U.S.C. §112, second paragraph

Claim 1 is rejected under 35 U.S.C. §112, second paragraph. The Examiner asserts that it failed to particularly point out and distinctly claim the subject matter which is regarded as the invention. In particular, the Examiner objected to the phrase "capable of". However, as set forth at Section 2173.05(g) of the MPEP concerning the use of such a phrase:

A functional limitation is an attempt to define something by what it does, rather than by what it is (*e.g.*, as evidenced by its specific structure or specific ingredients). There is nothing inherently wrong with defining some part of an invention in functional terms. Functional language does not, in and of itself, render a claim improper. *In re Swinehart*, 439 F.2d 210, 169 USPQ 226 (CCPA 1971).

2173.05(g)

Further, the MPEP cites an example paralleling our use of this functional definition:

It was held that the limitation used to define a radical on a chemical compound as "incapable of forming a dye with said oxidizing developing agent" although functional, was perfectly acceptable because it set definite boundaries on the patent protection sought. *In re Barr*, 444 F.2d 588, 170 USPQ 33 (CCPA 1971).

2173.05(g)

Likewise, the boundaries of the current invention can also be readily identified.

Additionally, it also appears that the Examiner is uncertain as to what elements are necessary for the invention to operate. The essential elements are that the composition be a polypeptide, that the polypeptide be androgenic—as defined in the art and the art itself limits any further narrowing (because of uncertainty in the field as to exactly what AGH is), and that the polypeptide be isolated (also a term of art for this hormone extract or part thereof).

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Rejections Under 35 U.S.C. § 101

Claims 10-11 stand rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter.

Claim 10 recites a population of shrimp or prawn having a skewed percentage of females to males, the population being made according to the method of Claim 6. Claim 6 requires breeding sexually reproductive neomale shrimp or prawn not containing transplanted androgenic tissue to produce the population recited by Claim 10. Independent Claim 11 is for a population of shrimp or prawns with a skewed percentage of females to males greater than about 90%.

The Examiner argues that Claims 10 and 11 read on a product of nature, and are therefore unpatentable subject matter. More specifically the Examiner argues that Claims 10 and 11 are interpreted as covering a population of normal shrimp or prawns. Applicants respectfully disagree.

Shrimp or prawn in nature do not naturally produce a skewed population of females to males such as would be covered by Claims 10 or 11. (See Malecha *et al*, 1992) Thus, for this reason alone Claims 10 and 11 do not cover a natural population of shrimp or prawn.

The Examiner asserts that the shrimp of claims 10 and 11 concern a population of wild-type shrimp because skewed (non-random) populations occur in nature.

Claims 10 and 11 are not directed to the individual shrimp, but rather to a population of shrimp. As such, a population having a skewed percentage of females to males of greater than 80-100% is statutory subject matter. It has not been shown that such skewed populations exist in nature. Absent some source to the contrary, any population of shrimp that is so biased by the method of claim 10 or 11 is not natural.

As additional support for the patenting of a skewed population, the Applicants would direct the Examiner to *In re Bergy*, 568 F.2d 1031, 195 USPQ 344 (CCPA 1977). In *Bergy*, the court held that all that was required to patent a population of organisms was that it be in a biologically pure form, not found in nature. The court looked at the fact that the organisms, as a population, did not exist in nature in such a pure form, and that the results could only be produced

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by carefully controlled laboratory conditions. In *Bergy*, the organisms themselves were not changed, only their state from nature was altered.

Additionally, the Examiner asserts that it is normal for ratios of males:females to vary from generation to generation; as such, the skewed nature of the present populations in claims 10 and 11 occurs in nature. While the Applicants appreciate the evolution based observation that the Examiner is making, the purpose of statistics and data analysis is to be able to define and understand significant changes from background (*i.e.* wild-type) breeding events. In the current field, such statistical analysis has been made in the area of breeding ratios (see Malecha *et al.* 1992) in sufficient detail as to be able to define how “skewed” a wild-type population can be, compared to how skewed the population of the present invention is. In fact, the fundamental assumption of Malecha’s paper (that breeding biases in nature are approximately random) proves that the event which the Examiner has mentioned is not the same as the breeding bias of the altered shrimp of claim 6. The difference between the Examiner’s assertion of a breeding bias and the bias in the current invention is recognized by the field as distinguishable by standard statistical analysis techniques. (see generally Malecha *et al.*) As such, while small “random” biases are routine, a bias of the magnitude discussed in claim 11 is not a natural event.

Rejections Under 35 U.S.C. § 103(a)

Claims 1-9 stand rejected under 35 U.S.C. § 103(a) as being obvious in light of Malecha *et al.*, in view of Okuno *et al.*; and Nagamine *et al.*

When rejecting claims under 35 U.S.C. § 103, the Examiner bears the burden of establishing a *prima facie* case of obviousness. See, *e.g.*, *In re Bell*, 26 USPQ2d 1529 (Fed. Cir. 1993); M.P.E.P. § 2142. To establish a *prima facie* case, three basic criteria must be met. First, the prior art reference, or references when combined, must teach or suggest each and every limitation of the rejected claims. See, *e.g.*, M.P.E.P. § 706.02(j). Second, the skilled artisan, in light of the teachings of the prior art, must have a reasonable expectation that the modification or combination suggested by the Examiner would be successful. See, *e.g.*, *In re Dow*, 5 USPQ2d 1529, 1531-32 (Fed. Cir. 1988). Finally, there must be some suggestion or motivation, either in

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the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify or combine the teachings of the reference in the manner suggested by the Examiner. See, e.g., *In re Grabiak*, 226 USPQ 870 (Fed. Cir. 1985). The teaching or suggestion to make the claimed invention, as well as the reasonable expectation of success, must come from the prior art, not Applicant's disclosure. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991); M.P.E.P. § 706.02(j). If any one of these criteria is not met, *prima facie* obviousness is not established.

1. References Do Not Teach Or Suggest Each Element Of The Claimed Invention

Claims 1-9 stand rejected under 35 U.S.C. § 103(a) as being obvious over Malecha *et al.* in view of Okuna *et al.* and Nagamine *et al.*

Claim 1 requires, *inter alia*, an isolated shrimp or prawn androgenic polypeptide capable of producing a sexually reproductive neomale shrimp or prawn. Claim 2 requires a sexually reproductive neomale shrimp or prawn which do not contain transplanted androgenic gland tissue. Claim 3 requires, *inter alia*, treating shrimp or prawn with a composition comprising an androgenic peptide to produce a sexually reproductive neomale shrimp or prawn. Claim 6 requires, *inter alia*, breeding a sexually reproductive neomale shrimp or prawn not containing transplanted androgenic gland tissue to produce a population of prawn or shrimp having skewed percentages of females to males.

The Examiner admits that Malecha *et al.* do not teach producing a neomale by treating a female shrimp with a composition comprising an androgenic polypeptide, as recited in the claimed invention. The Examiner argues that this deficiency is made up by the teachings of Okuna *et al.* in combination with the teachings of Nagamine *et al.* More specifically, the Examiner argues that the teaching by Okuna *et al.*—AGH masculinizes *Armadillidium vulgare*, (an isopod) , in combination with the suggestion by Nagamine *et al.*—the androgenic glands (AG) of *isopods*, *decapods*, *amphipods* may function similarly—render it obvious to treat a female shrimp or prawn (decapods) with an androgenic polypeptide to produce a sexually reproductive neomale shrimp or prawn. Applicants respectfully disagree.

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Malecha *et al.* teach a method of producing sexually reproductive neomale prawn by implanting the androgenic gland of a male prawn into a female prawn. Further, Malecha *et al.* teach a method of crossbreeding these neomale prawns with normal females to produce a population having a skewed percentage of females to males. Significantly, Malecha *et al.* do not teach or suggest an isolated shrimp or prawn androgenic polypeptide capable of producing a sexually reproductive neomale, nor a method of using the polypeptide to produce a sexually reproductive neomale.

Okuna *et al.* do not make up for the deficiencies of Malecha *et al.* Okuna *et al.* teach the purification of an androgenic hormone extract (AGH) from isolated androgenic glands of *A. vulgare*, a terrestrial isopod. Further, Okuna *et al.* teach that injecting 38pg of the AGH extract into female *A. vulgare* results in "masculinization." "Masculinization" is defined by Okuno *et al.* as being limited to elongation of the endopodites of the first pair of abdominal legs. Masculinization, as defined by Okuno *et al.*, is significantly different from formation of a sexually reproductive neomale, as recited by the claims. Significantly, Okuna *et al.* never produce a sexually reproductive neomale *A. vulgare* (isopod), let alone a sexually reproductive neomale shrimp or prawn (decapod).

Nagamine *et al.*, alone or in combination with Okuna *et al.*, also do not make up for the deficiencies of Malecha *et al.* Nagamine *et al.* teach transplanting *M. rosenbergii* (decapod) androgenic glands (AG) into females of the same species. Significantly, the transplantation taught by Nagamine *et al.* resulted only in masculinization and never resulted in a sexually reproductive neomale.

Thus, the references, taken alone or in any combination, do not teach or suggest an isolated shrimp or prawn androgenic polypeptide capable of producing a sexually reproductive neomale, nor the production of a sexually reproductive neomale shrimp or prawn using the androgenic polypeptide, as required by the claimed invention. Therefore, the references, taken alone or in any combination, do not teach or suggest each and every element of Claims 1-9. For this reason alone the Examiner has failed to make out a *prima facie* case of obviousness against Claims 1-9.

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However, the issue of reproductive neomales vs. masculinized shrimp is not the only element absent from the prior art. The hormone itself (AGH) could not have been taught as an element because there was no consensus in the field as to what constituted the actual hormone. Different groups have characterized “the AGH” molecule of isopods and decapods as:

- i) a lipophilic compound or as a protein,
- ii) a single entity, a dual entity, a four subunit entity—each part with or without activity,
- iii) expressed in the incorrect location and not in the required location
- iv) as being heat stabile or not being heat stabile,
- v) as having or not having disulfide bonds
- vi) as a molecule with a molecular weight ranging anywhere from 2000 to 18,900 and
- vii) with a specific activity ranging up to 1870 fold greater than other samples of the “same” hormone (*see generally* Okuno 837-842 (1997)).

Because of these huge variations in the field, it is improper for the Examiner to claim that the desired invention was simply a matter of combining a “known” hormone obtained by a “known” method in a distantly related organism. The uncertainty in the field is emphasized by the recent retractions of previous results claiming to have isolated AGH (as in Okuno *et al.* 1997) and by the fact that papers have been published (after the submission of this application) concerning disagreements over purification and characteristics of AGH. (Okuno, 1999). Considering the ongoing debate about the hormone in isopods (*A. vulgare*) alone, and thus, how to purify it, it is submitted that, to those skilled in the art, the selection of the proper isolation process is not an obvious one, especially when one uses the process on a different organism.

In addition, the MPEP (2121.02) cites *In re Hoeksema* 399 F.2d 269 in which the court held that the mere naming of an element, without actual identification of the element is insufficient for enablement. Additionally, in *In re Wiggins* 488 F2d 538, the court held that the existence of previous failures, is adequate to show inoperability of the prior art. Given the ongoing debate about the above mentioned characteristics of AGH, the Applicants submit that at the time of the

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submission of this application AGH was not actually identified in any meaningful way. Indeed, the large disagreements in the prior art establishes the inoperability of the prior art itself.

For these reasons the Examiner has failed to make out a *prima facie* case of obviousness against Claims 1-9.

2. The References Do Not Provide A Reasonable Expectation Of Success

The references, taken alone or in any combination, do not provide the skilled artisan with any reasonable expectation of successfully producing a sexually reproductive neomale shrimp or prawn from an isolated androgenic polypeptide. The Examiner asserts that one skilled in the art would expect the combination of a technique which worked for an isopod (*A. vulgare*), to work for a decapod, namely that isolation techniques between the two organisms would be equivalent. The Applicants disagree.

The prior art contradicts the Examiner's assertion regarding the expectation of success. The prior art has stated that these organisms are not equivalent; in particular, attempts to isolate AGH from decapods and isopods have yielded different results (1st paragraph, p352 Katakura *et al.*, *Monitore zool. ital.* 4:351-358 (1989)). Since the art explicitly recognizes this difference between the AGH proteins and isolation techniques of isopods (*A. vulgare*) and decapods, one skilled in the art would not have had a reasonable expectation of success doing what the Examiner has proposed.

In addition, *A. vulgare*, an isopod, commonly known as the "rollie-pollie" or "pillbox bug", is a terrestrial organism, often found in gardens, breathes air, and does not live in water. On the other hand, *M. rosenbergii*, a decapod, commonly known as the prawn, lives in water, and does not breath air. These huge environmental differences alone would suggest to one skilled in the art that the characteristics of each of the organisms are different, not to mention the obvious differences due to different organs present in each of the organisms.

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In addition, these two organisms are not of the same species, genus, family, or order, but only of similar class. For perspective, this relationship would also equate a process for purification of a protein from barnacles, krill (*i.e.* plankton), woodlice, and lobsters since all are in the same class.

Additionally, as discussed, Okuna *et al.* merely masculinized *A. vulgare* (isopod), by injecting *A. vulgare* AGH extract into a female of the same species.

At best Malecha *et al.*, in view of Okuno *et al.* and Nagamine *et al.* piques the skilled artisan's curiosity for further experimentation. However, it has been "consistently held that 'obvious to try' is not to be equated with obviousness" *The Gillette Co. v. S.C. Johnson & Son Inc.*, 16 USPQ2d 1923, 1928 (Fed. Cir. 1990).

None of the references, taken alone or in any combination, provide an adequate disclosure to successfully isolate shrimp or prawn androgenic polypeptide capable of producing a sexually reproductive neomale, or to successfully produce a sexually reproductive neomale shrimp or prawn using the polypeptide. For this additional reason the Examiner has failed to establish a *prima facie* case of obviousness against Claim 1-9.

3. Conclusion

Applicants respectfully submit that the Examiner has failed to make out a *prima facie* case of obviousness against Claims 1-9. More specifically, the references, taken alone or in combination, do not teach or suggest each and every element of the claimed invention. Moreover, none of the references, taken alone or in any combination, provide a reasonable expectation of successfully producing a sexually reproductive neomale shrimp or prawn by using an androgenic polypeptide. Accordingly, Applicants respectfully request the Examiner to withdraw the rejection of Claims 1-9 under 35 U.S.C. § 103(a) as being obvious over Malecha *et al.* in view of Okuno *et al.* and Nagamine *et al.*

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CONCLUSION

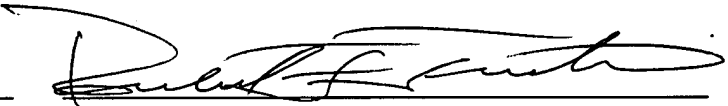
Applicant respectfully submits that Claims 1-11 satisfy all of the requirements for patentability and are in condition for allowance. Early passage to issuance of these claims is therefore kindly solicited.

If the Examiner has further unresolved issues after considering this amendment, the Examiner is respectfully requested to phone the undersigned attorney.

Respectfully submitted,

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